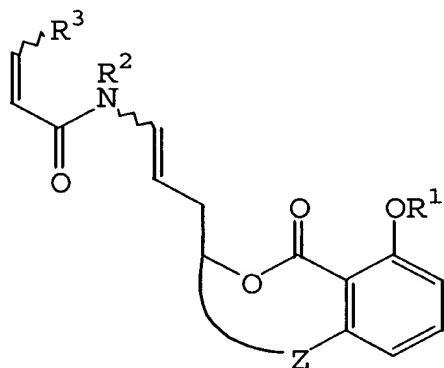


CLAIMS

1. (Previously Presented) A method of treating or preventing a condition treatable by the inhibition of vacuolar-type (H⁺)-ATPase, said method comprising administering to a patient a vacuolar-type (H⁺)-ATPase inhibiting-effective amount of at least one compound of the formula:



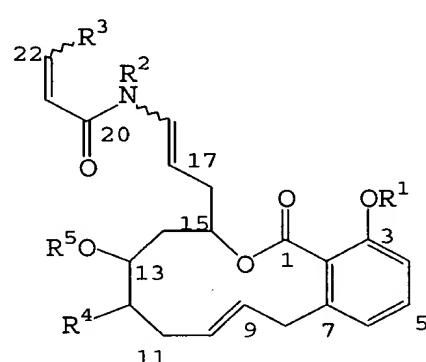
(I),

wherein R¹ and R² are the same or different and each is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, R⁶CH₂-, R⁶CO-, or R⁶SO₂-, wherein R⁶ is H, a straight-chain or branched saturated or unsaturated alkyl, or an aryl; R³ is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, an oxime, or an oxime methyl ether; the aromatic ring is unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano; the saturated alkyl, unsaturated alkyl and aryl substituents defined in R¹-R³ and R⁶ are unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano; and Z is a contiguous linker comprising a chain of 0-12 atoms which, together with the five atoms beginning with the carbon of the aromatic ring of formula (I) in meta-relationship with OR¹ and ending with the carbon directly attached to the alkyl oxygen of the lactone of formula (I), said carbons being covalently bonded to either end of linker Z, integrally form a 5-17 membered ring; or a pharmaceutically acceptable salt, an ester, or a prodrug thereof, provided that the condition is not cancer.

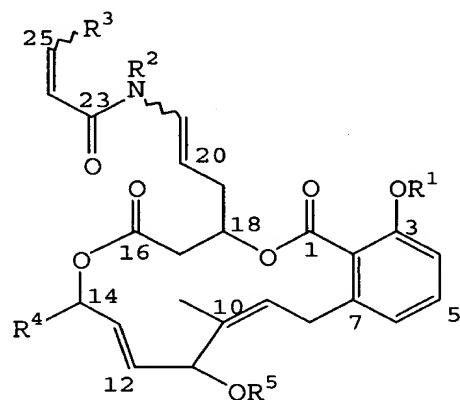
2. (Previously Presented) The method of claim 1, wherein Z is a contiguous linker comprising a chain of 7-12 atoms which, together with the five atoms beginning with the carbon of the aromatic ring of formula (I) in meta-relationship with OR¹ and ending with

the carbon directly attached to the alkyl oxygen of the lactone of formula (I), said carbons being covalently bonded to either end of linker Z, integrally form a 12-17 membered ring.

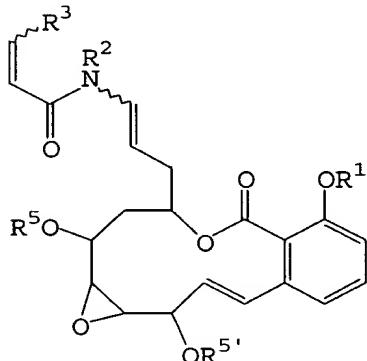
3. (Previously Presented) The method of claim 1, wherein said compound is selected from the group consisting of:



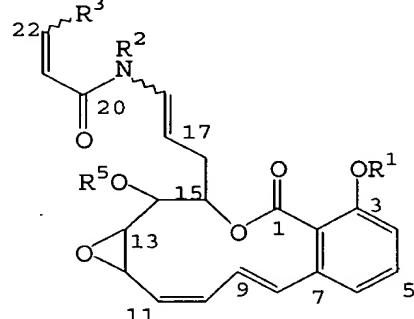
(IA),



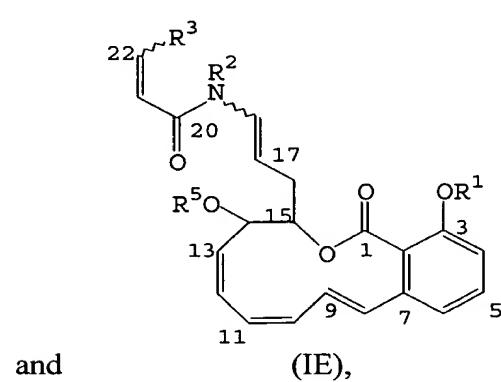
(IB),



(IC),



(ID),

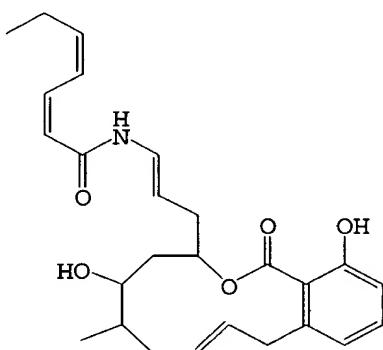


and

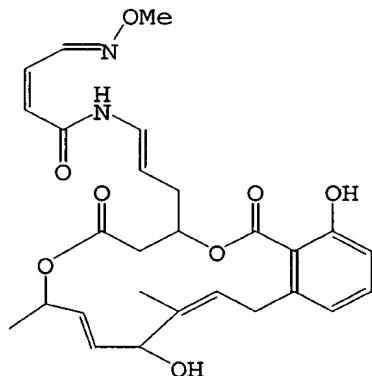
(IE),

wherein R¹ and R² are the same or different and each is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, R⁶CH₂-, R⁶CO-, or R⁶SO₂-, wherein R⁶ is H, a straight-chain or branched saturated or unsaturated alkyl, or an aryl; R³ is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, an oxime, or an oxime methyl ether; R⁴ is H, an alkyl, or R⁷CH₂-, wherein R⁷ is R⁶O-, R⁶CO₂-, or R⁶SO₃-, R⁵ and R^{5'} are the same or different and each is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, a glycoside, R⁶CH₂-, R⁶CO-, or R⁶SO₂-, the saturated alkyl, unsaturated alkyl and aryl defined in R¹-R³, R⁵, R^{5'} and R⁶, and the alkyl defined in R⁴, are unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano; and the aromatic ring of formula (I) is unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano; or a pharmaceutically acceptable salt, an ester, or a prodrug thereof.

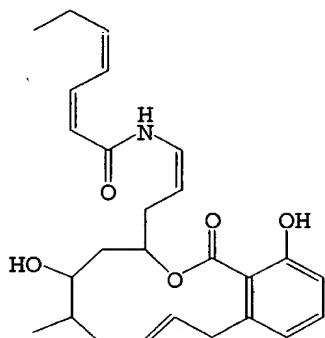
4. (Previously Presented) The method of claim 3, wherein said compound is selected from the group consisting of:



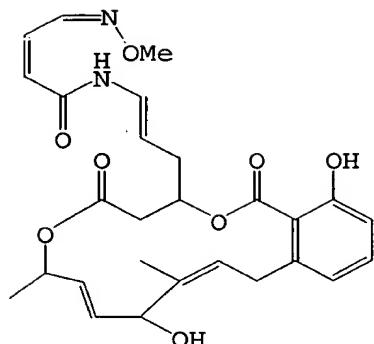
salicylihalamide A,



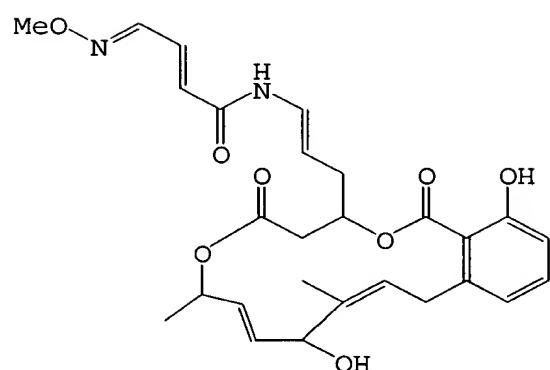
lobatamide A,



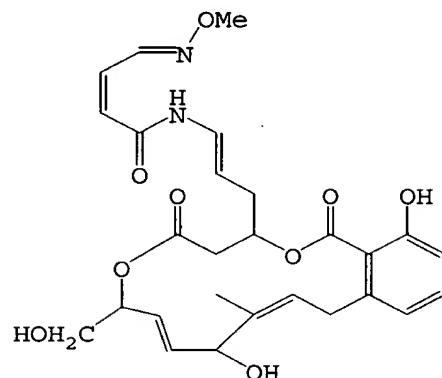
salicylihalamide B,



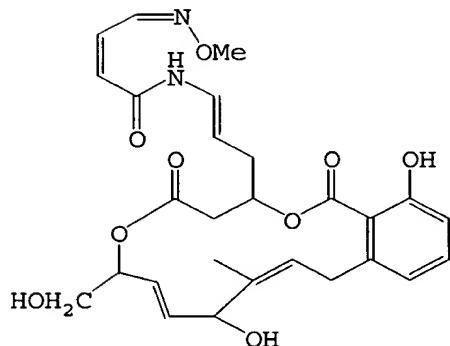
lobatamide B,



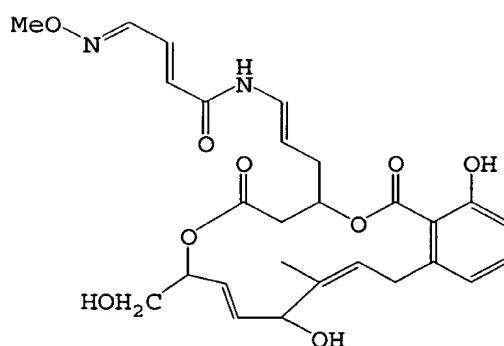
lobatamide C,



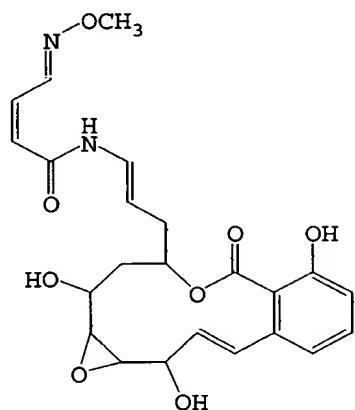
lobatamide D,



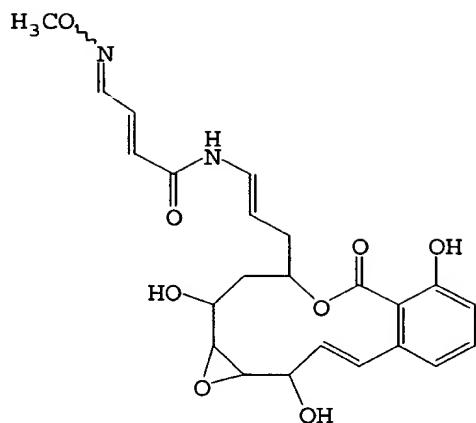
lobatamide E,



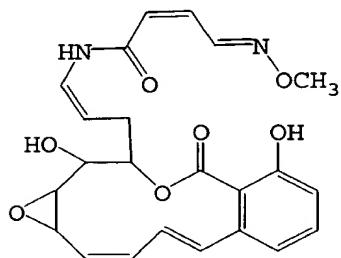
lobatamide F,



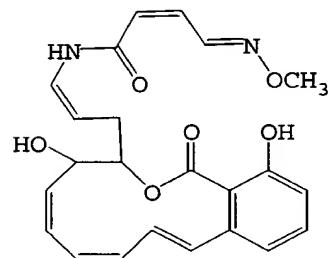
CJ-12,950,



CJ-13,357,



oximidine 1,

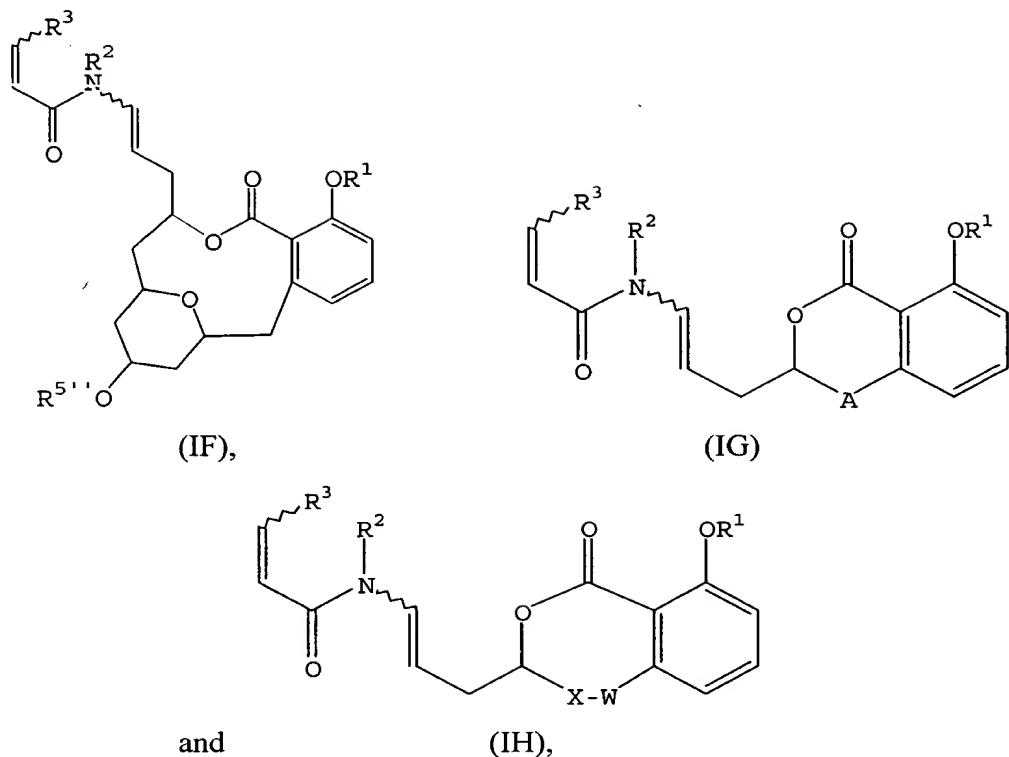


and oximidine 2;

or a pharmaceutically acceptable salt, an ester, or a prodrug thereof.

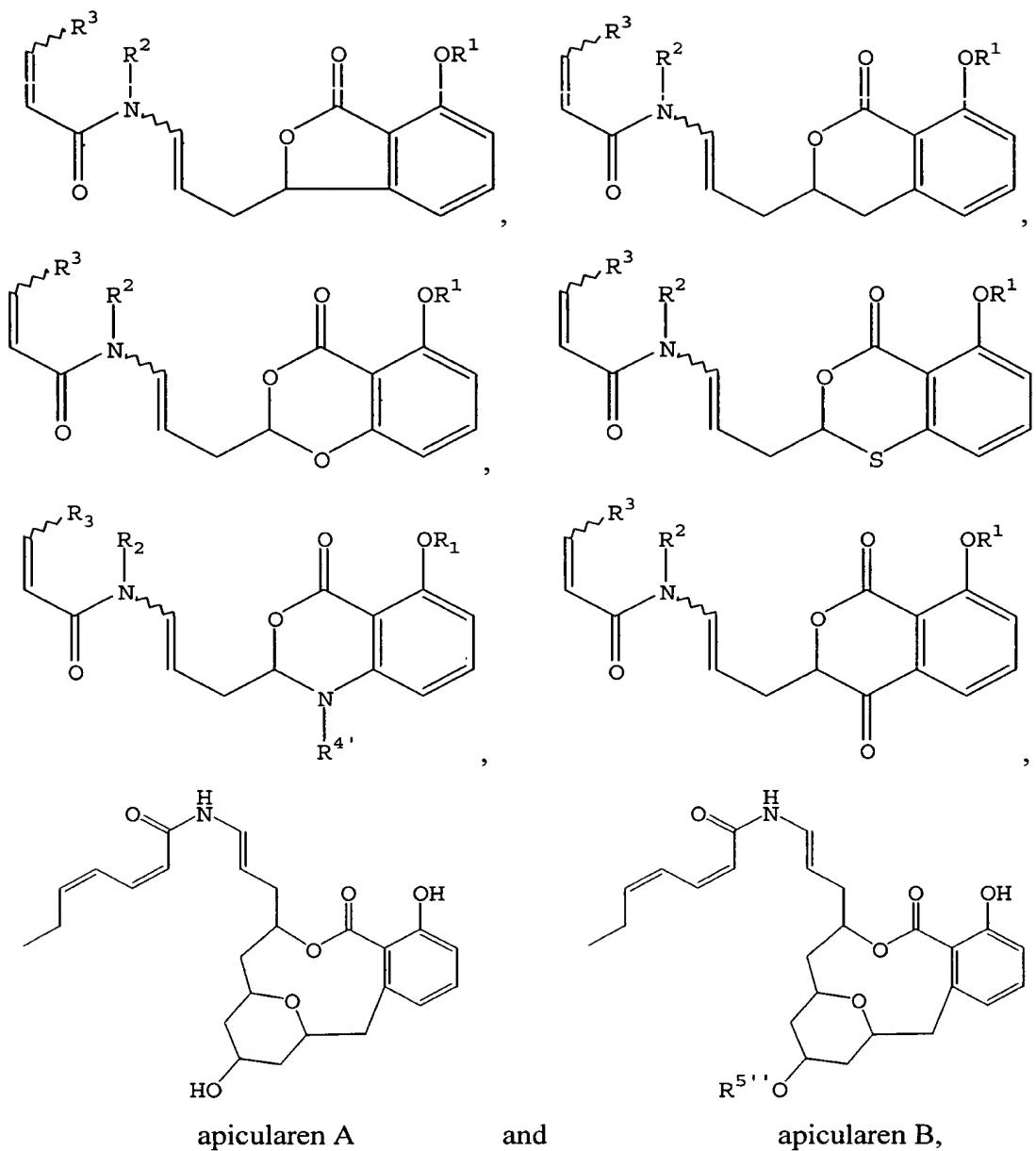
5. (Previously Presented) The method of claim 1, wherein Z is a contiguous linker comprising a chain of 0-6 atoms which, together with the five atoms beginning with the carbon of the aromatic ring in meta-relationship with OR¹ and ending with the carbon directly attached to the alkyl oxygen of the lactone, said carbons being covalently bonded to either end of linker Z, integrally form a 5-11 membered ring.

6. (Previously Presented) The method of claim 1, wherein said compound is selected from the group consisting of:



wherein $\text{R}^1\text{-R}^3$ are as defined in claim 1; $\text{R}^{5''}$ is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, a glycoside, $\text{R}^6\text{CH}_2\text{-}$, $\text{R}^6\text{CO-}$, or $\text{R}^6\text{SO}_2\text{-}$, wherein R^6 is as defined in claim 1; the saturated alkyl, unsaturated alkyl and aryl defined in $\text{R}^{5''}$ are unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano; A is a covalent bond or a $\text{C}_1\text{-C}_6$ straight-chain saturated or unsaturated alkyl linker which is unsubstituted or is substituted with a one or more substituents selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano; X is a covalent bond or a $\text{C}_1\text{-C}_5$ straight-chain saturated or unsaturated alkyl linker which is unsubstituted or is substituted with a one or more substituents selected from the group consisting of a halogen, a nitro, an amino, hydroxyl, thio, acyl, $\text{C}_1\text{-C}_6$ alkyl, and cyano; and W is O, S, $\text{C}(\text{O})$, $\text{C}(\text{S})$, $\text{S}(\text{O})_n$ or $\text{N}-\text{R}^4$, wherein R^4 is H, $\text{C}_1\text{-C}_6$ straight-chain or branched saturated or unsaturated alkyl, aryl, $\text{R}^6\text{CH}_2\text{-}$, $\text{R}^6\text{CO-}$, or $\text{R}^6\text{SO}_2\text{-}$, R^6 is as defined in claim 1, and n is an integer from 0-2.

7. (Previously Presented) The method of claim 6, wherein said compound is selected from the group consisting of:



wherein R^{5'''} is N-acetyl- β -D-glucosamine.

8. (Previously Presented) The method of claim 1, which further comprises co-administering to a patient in need thereof a therapeutically effective amount of at least one additional compound other than a compound defined in any of claim 1.

9. (Previously Presented) The method of claim 8, wherein said additional compound is selected from the group consisting of bafilomycins and concanamycins.

10. (Previously Presented) The method of claim 9, wherein said additional compound is concanamycin A.

11. (Previously Presented) The method of claim 9, wherein said additional compound is baflomycin A₁.

12. (Previously Presented) The method of claim 1, wherein said vacuolar-type (H⁺)-ATPase inhibiting-effective amount is effective to inhibit intra-organellar acidification of intracellular organelles.

13. (Previously Presented) The method of claim 1, wherein said vacuolar-type (H⁺)-ATPase inhibiting-effective amount is effective to inhibit urinary acidification.

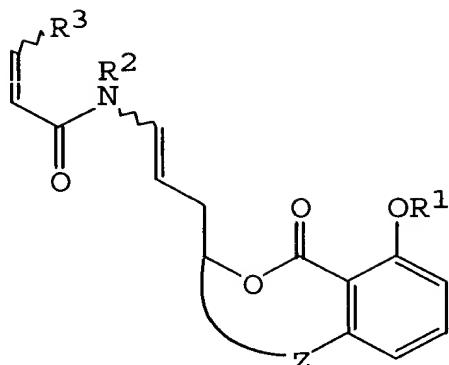
14. (Previously Presented) The method of claim 1, wherein said vacuolar-type (H⁺)-ATPase inhibiting-effective amount is effective to inhibit bone resorption.

15. (Previously Presented) The method of claim 14, wherein said vacuolar-type (H⁺)-ATPase inhibiting-effective amount is effective to treat osteoporosis.

16. (Previously Presented) The method of claim 1, wherein said vacuolar-type (H⁺)-ATPase inhibiting-effective amount is effective to inhibit fertility.

17. (Previously Presented) The method of claim 1, wherein said vacuolar-type (H⁺)-ATPase inhibiting-effective amount is effective to inhibit angiogenesis.

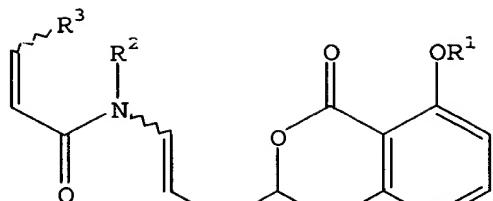
18. (Previously Presented) A composition comprising a vacuolar-type (H⁺)-ATPase inhibiting-effective amount of at least one compound of the formula:



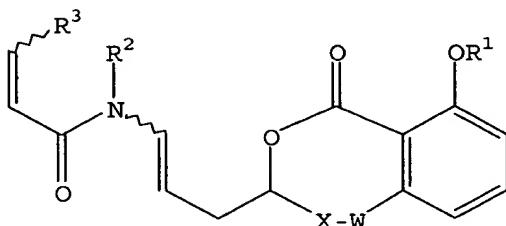
(I),

wherein R¹ and R² are the same or different and each is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, R⁶CH₂-, R⁶CO-, or R⁶SO₂-, wherein R⁶ is H, a straight-chain or branched saturated or unsaturated alkyl, or an aryl; R³ is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, an oxime, or an oxime methyl ether; the saturated alkyl, unsaturated alkyl and aryl substituents defined in R¹-R³ and R⁶ are unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano; the aromatic ring is unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano; and Z is a contiguous linker comprising a chain of 0-6 atoms which, together with the five atoms beginning with the carbon of the aromatic ring of formula (I) in meta-relationship with OR¹ and ending with the carbon directly attached to the alkyl oxygen of the lactone of formula (I), said carbons being covalently bonded to either end of linker Z, integrally form a 5-11 membered ring; or a pharmaceutically acceptable salt, an ester, or a prodrug thereof; and a pharmaceutically acceptable carrier; provided that the compound is not apicularen A or B.

19. (Previously Presented) The composition of claim 18, wherein said compound is selected from the group consisting of:



(IG)

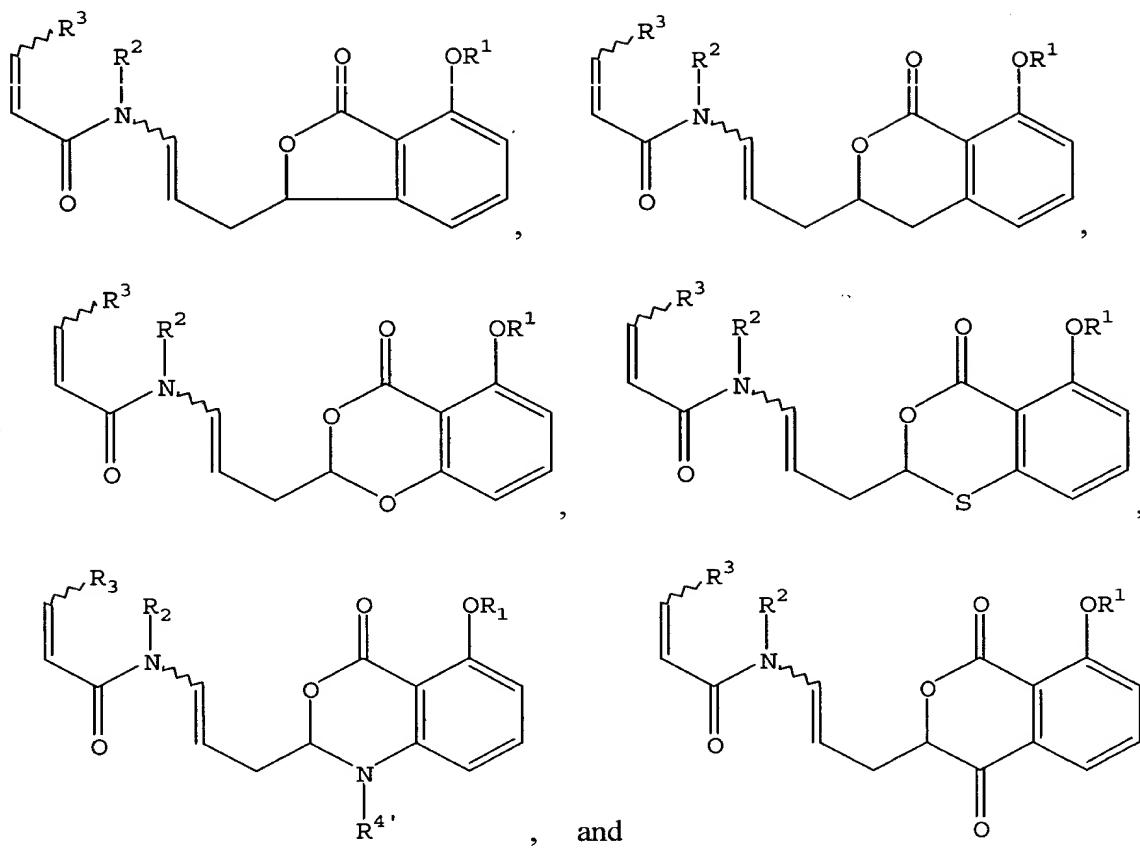


and

(IH),

wherein R^1-R^3 are as defined in claim 18; A is a covalent bond or a C_1-C_6 straight-chain saturated or unsaturated alkyl linker which is unsubstituted or is substituted with a one or more substituents selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano; X is a covalent bond or a C_1-C_5 straight-chain saturated or unsaturated alkyl linker which is unsubstituted or is substituted with a one or more substituents selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano; and W is O , S , $C(O)$, $C(S)$, $S(O)_n$ or $N-R^4$, wherein R^4 is H , a straight-chain or branched saturated or unsaturated alkyl, an aryl, $R^6\text{CH}_2-$, $R^6\text{CO}-$, or $R^6\text{SO}_2-$, wherein R^6 is as defined in claim 18 and n is an integer from 0-2.

20. (Previously Presented) The composition of claim 19, wherein said compound is selected from the group consisting of:



21. (Previously Presented) The composition of claim 18, which further comprises a vacuolar-type (H⁺)-ATPase inhibiting effective amount of at least one additional compound other than a compound defined in claim 18.

22. (Previously Presented) The composition of claim 21, wherein said additional compound is selected from the group consisting of baflomycins and concanamycins.

23. (Previously Presented) The composition of claim 22, wherein said additional compound is concanamycin A.

24. (Previously Presented) The composition of claim 22, wherein said additional compound is baflomycin A₁.

25. (Previously Presented) The composition of claim 18, wherein said vacuolar-type (H⁺)-ATPase inhibiting-effective amount is effective to inhibit intra-organellar acidification of intracellular organelles.

26. (Previously Presented) The composition of claim 18, wherein said vacuolar-type (H⁺)-ATPase inhibiting-effective amount is effective to inhibit urinary acidification.

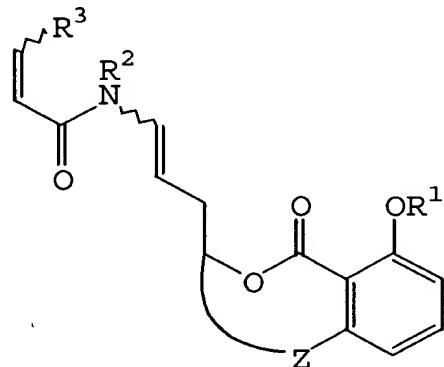
27. (Previously Presented) The composition of claim 18, wherein said vacuolar-type (H⁺)-ATPase inhibiting-effective amount is effective to inhibit bone resorption.

28. (Previously Presented) The composition of claim 27, wherein said vacuolar-type (H⁺)-ATPase inhibiting-effective amount is effective to treat osteoporosis.

29. (Previously Presented) The composition of claim 18, wherein said vacuolar-type (H⁺)-ATPase inhibiting-effective amount is effective to inhibit fertility.

30. (Previously Presented) The composition of claim 18, wherein said vacuolar-type (H⁺)-ATPase inhibiting-effective amount is effective to inhibit angiogenesis.

31. (Previously Presented) A method of treating or preventing a condition treatable by the inhibition of vacuolar-type (H⁺)-ATPase, said method comprising administering to a patient a vacuolar-type (H⁺)-ATPase inhibiting-effective amount of at least one compound of the formula:



(I),

wherein R¹ and R² are the same or different and each is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, R⁶CH₂-, R⁶CO-, or R⁶SO₂-, wherein R⁶ is H, a straight-chain or branched saturated or unsaturated alkyl, or an aryl; R³ is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, an oxime, or an oxime methyl ether; the aromatic ring is unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano; the saturated alkyl, unsaturated alkyl and aryl substituents defined in R¹-R³ and R⁶ are unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano; and Z is a contiguous linker comprising a chain of 0-6 atoms which, together with the five atoms beginning with the carbon of the aromatic ring in meta-relationship with OR¹ of formula (I) and ending with the carbon directly attached to the alkyl oxygen of the lactone of formula (I), said carbons being covalently bonded to either end of linker Z, integrally form a 5-11 membered ring; or a pharmaceutically acceptable salt, an ester, or a prodrug thereof, provided that the compound is not apicularen A or B.